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Parotid Metastasis of Renal Cell Carcinoma: A Case Report and Review of the Literature

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Abstract

Background: To review the presentation and management of renal cell carcinoma metastatic to the parotid gland.

Methods: Case report and review of the literature.

Results: There have been 45 cases of renal cell carcinoma metastatic to the parotid gland reported in the English literature. A parotid lesion can be the initial clinical presentation of this malignancy (even before primary site identification). A case of patient with a parotid mass noted 4 years after undergoing a nephrectomy for renal cell carcinoma is presented. Superficial parotidectomy with facial nerve monitoring demonstrated metastatic renal cell carcinoma with negative margins on pathology.

Conclusions: Metastatic renal cell carcinoma should be considered in the differential diagnosis a vascular parotid mass in patients have a history of prior diagnosis of renal cell carcinoma. After diagnosis is established, a systemic assessment should be performed given that solitary parotid metastases are uncommon. Due to the limited number of cases reported in the literature, clinical outcomes are difficult to predict.

Keywords: renal cell carcinoma, parotid metastases, parotidectomy, distant metastasis.

Background

Malignancies of the parotid gland are relatively uncommon, accounting for only 3-6% of all head and neck cancers and 0.3% of all cancers [1]. Approximately 30% of parotid tumors are malignant and most represent primary salivary gland tumors. Metastatic spread to the parotid is uncommon but should be considered at the time of initial assessment of a parotid mass. The most common primary malignancies associated with metastasis to the parotid are cutaneous neoplasms of the head and neck [2]. However, ductal carcinoma of the breast, rhabdomyosarcoma, small cell carcinoma of the lung, and renal cell carcinoma are also primary tumors that harbor the potential for metastatic spread to the parotid that have been reported [2,3].

Renal cell carcinoma (RCC) is a relatively uncommon cancer with approximately 54,000 new cases and 13,000 deaths noted annually in the United States. It has a 3:2 male predominance and a peak incidence in the 6th and 7th decades of life. Though tobacco use, obesity, and hypertension are the only identified risk factor, most cases are sporadic. The classic triad of clinical presentation includes hematuria, pain, and abdominal mass, however greater than 50% of cases are detected incidentally during abdominal imaging for another indication [4].

RCC is well known for its unique potential to metastasize to nearly every organ system in the body. The tumor is highly vascular and thought to metastasize via both hematogenous (via the Batson's plexus) and lymphatic routes [5]. The most common sites for metastasis are the lung, bone, adrenal, liver, brain, and the contralateral kidney [4]. Though not as frequent, metastatic RCC to the head and neck has been identified in the thyroid, salivary glands, skull base, sinuses, pharynx, tonsils, tongue, lip and skin [6]. Metastasis to the parotid gland is very rare. In a study by Bernicker et al of 65 patients with RCC metastasis to the head and neck, none of the patients presented with parotid metastasis [6]. The first case of RCC metastatic to the parotid gland was published by Patey et al in 1965 [7]. Since then there have only been 45 reported cases reported in the English literature [5,7-37,39]. Although this entity is uncommon in presentation, this review highlights issues that may assist the head and neck surgeon with a pathologic diagnosis not often encountered cephalad to the clavicles.

Methods

PubMed and MEDLINE were used to search the English literature database (from 1965-2011) using the terms "renal cell carcinoma" and "parotid gland." References from those articles were thoroughly reviewed. Only relevant publications were included. Cases of renal cell carcinoma metastatic to the parotid gland were reviewed with emphasis on patient age, gender, presenting symptoms and duration, time interval since diagnosis of primary cancer, physical exam, diagnostic tests results including fine needle aspiration (FNA), radiologic

imaging, pathologic diagnosis, management, other sites of distant metastasis, and postoperative outcome. Finally, the author's case report of renal cell carcinoma metastatic to the parotid gland was retrospectively reviewed with attention to clinic notes, operative notes, radiology, and pathology reports and is presented below.

Results

Case report

A 71 year-old man was referred for management of a right parotid mass that was first noticed 2 years prior. Over the preceding 12 months the mass had become increasingly tender after being accidentally traumatized. The patient denied any significant change in size of the mass, paresthesia, or facial weakness. There was no associated dysphagia, hoarseness, otalgia, dyspnea, or unexplained weight loss. He had a past medical history significant for hypertension. Of note, the patient had undergone a right nephrectomy 5 years prior for renal cell carcinoma. The patients also had a 50+ pack-year smoking history and denied a family history of renal diagnoses or other cancer syndromes.

On physical exam, there was a non-tender, soft mass in the tail of the right parotid without associated lymphadenopathy. The patient's body-mass index (BMI) was 24.33 and blood pressure was 145/65 during evaluation. Both computed tomography (CT) scan (**Figure 1** & **2**) and magnetic resonance imaging (MRI) of the neck with contrast had been performed prior and showed an isolated right-sided lobular parotid mass that measured 3.0 x 2.4 x 2.5cm. Of note, the mass demonstrated an intense uptake of contrast. On repeat MRI at the time of evaluation there was noted to be an interval increase of the mass to 3.5 x 3.2 x 3.7 cm. The patient underwent a total parotidectomy with facial nerve preservation. Intraoperative facial nerve 4-channel monitoring was utilized.

On pathologic review, the parotid was noted to harbor a soft, well-encapsulated, orange-tan, homogenous well-circumscribed lesion with areas of hemorrhage (**Figure 3**). The tumor appeared to be confined within a thin capsule. The remainder of the specimen demonstrated normal parotid tissue. Histological evaluation demonstrated polygonal to round cells with abundant clear cytoplasm and large nucleoli containing small nucleoli (**Figure 2**), in a stark contrast to normal parotid tissue (**Figure 4**). Immunohistochemistry revealed positive staining for vimentin (**Figure 5**) and CD10 (**Figure 6**), which lead to the diagnosis of renal cell carcinoma metastatic to the parotid gland.

Following this diagnosis, the patient underwent full-body imaging which demonstrated 3 small lesions in the pancreas that were stable compared to prior imaging. One year after the surgery, the patient was doing well and remained disease-free.

Review of literature.

The English literature reports 45 cases of RCC metastatic to the parotid gland since 1965 [**5**,**7**-**37**,**39**]. Only 31 complete case presentations have been documented (**Table 1**).

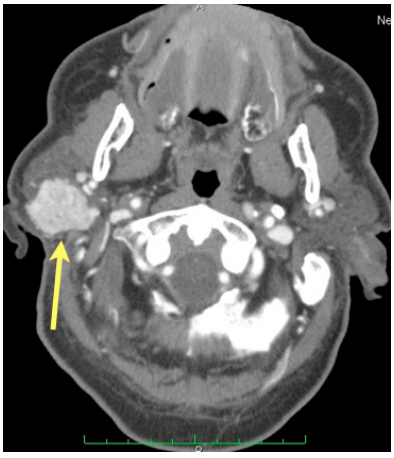

Figure 1. Axial and coronal views of a CT scan with contrast of the neck demonstrating a vascular lesion within the superficial aspect of the right parotid gland.

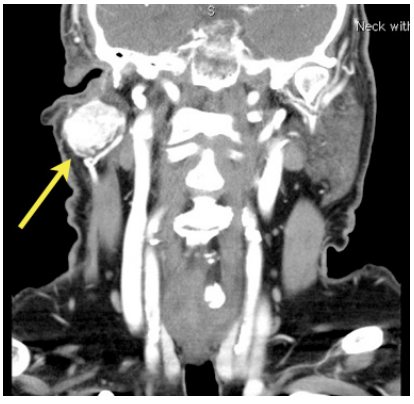

Figure 2. Axial and coronal views of a CT scan with contrast of the neck demonstrating a vascular lesion within the superficial aspect of the right parotid gland.

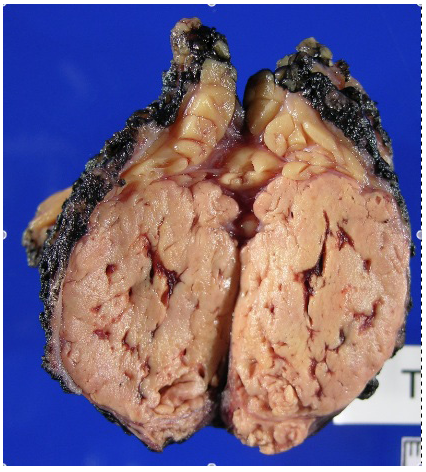

Figure 3. Right superficial parotidectomy gross specimen.

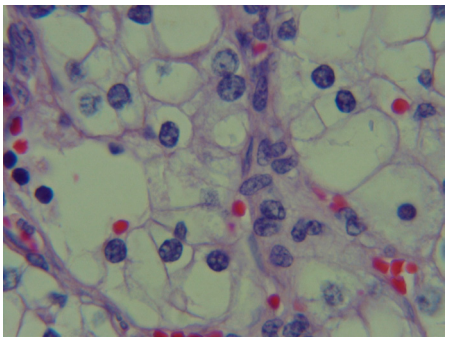

Figure 4. Hematoxylin and eosin stain of carcinoma cells. Note the optically clear cytoplasm and large slightly basophilic nuclei containing small nucleoli.

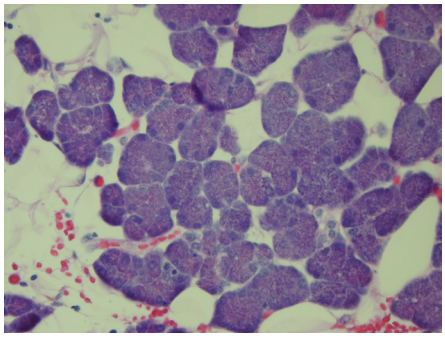

Figure 5. Hematoxylin and eosin stain of normal parotid tissue demonstrating acini and granular cytoplasm.

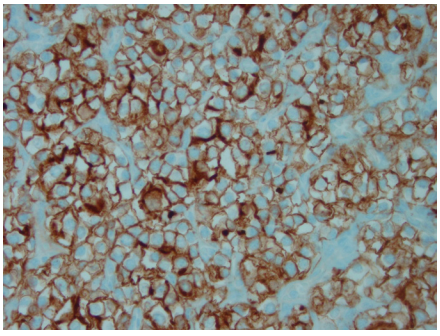

Figure 6. Strongly positive vimentin immunohistochemical stain in carcinoma cells.

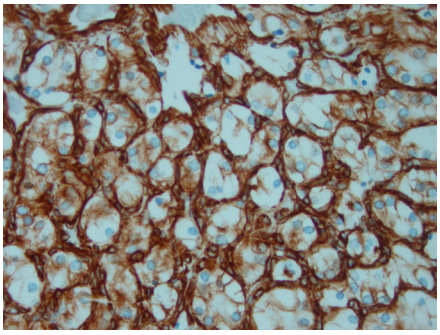

Figure 7. Strongly positive CD10 immunohistochemical stain in carcinoma cells.

[5,7-11,13-17,19,20,22-30,32-35,39]. There was a 2:1 male predominance. Age ranges from 42-83, with a mean of 61.9 (±9.5). Twenty-nine of the patients presented with unilateral parotid metastasis. Sarangi *et al.* [23] described a patient that initially presented with a left parotid mass and developed a right parotid mass 4 months later. Ravi *et al.* [22] reported a case of bilateral parotid metastases. All of the patients had a palpable mass on presentation and 19 of the patients were asymptomatic. Associated symptoms included painful or tender masses (7), pulsatile mass (2), bruit over mass (1), tinnitus (1), ipsilateral facial weakness (1), and numbness of the ipsilateral commissure of the lip (1).

In 16 of the cases, parotid metastasis was the first sign of the renal primary. Fourteen of the patients had been diagnosed and treated for RCC in prior to parotid metastasis with an interval prior parotid presentation that spanned from 5 months to 19 years. Wayne *et al.* [9] reported a patient that was diagnosed with RCC of the parotid but no primary tumor was ever identified. In 16 of the cases, the patients were found to have metastatic disease beyond the parotid upon subsequent work-up. Four patients appeared to have isolated parotid disease at the time of their presentation but went on to develop other distant metastatic disease. There were 4 cases of isolated parotid metastasis. Seven reports did not discuss distant metastasis.

Fine needle aspiration was performed in 13 of the reported cases. It was diagnostic in 3, non-diagnostic in 10, and not mentioned in 18 of the published cases. Twenty-eight of the patients underwent excision of the parotid disease. Fifteen patients underwent superficial parotidectomies, 1 underwent a partial parotidectomy, 1 underwent a "deep" parotidectomy, and 5 underwent total parotidectomy. The remaining 6 authors did not detail the extent of the procedure beyond excision of the mass. Three authors elected to perform neck dissections in addition to parotidectomy. 11 authors mentioned the facial nerve with preservation noted in 10 of the cases. In 1 case the inferior portion of the facial nerve required sacrifice for complete resection of the tumor. There were 3 reports of locally recurrent disease after excision. Two patients were not managed with palliative intent with radiotherapy and pain relief. One author did not comment on therapy.

Eight of the articles published since 1989 described immunohistochemical stains used to identify the primary tumor (**Table 1**) [9,11-14,20,28,39]. RCC consistently stained positive for proximal nephron renal antigen (PNRA), vimentin, CD10, and cytokeratin (CAM5.2). Common negative stains were carcinoembryonic antigen (CEA) and cytokeratin-7.

Discussion

Metastasis from RCC to the parotid gland is a rare finding. RCC also poses a particular diagnostic challenge because distant disease can present synchronous with the diagnosis of the primary renal tumor or a metachronous distant presentation may occur many years after therapy for the primary. For greater than 50% of the case presentations reviewed, the parotid lesion was

Table 1. Summary of all complete case presentations of RCC metastatic to the parotid gland dating from 1965 to present.
R.: right, L.: left, RCC: renal cell carcinoma, mets: metastasis

Author	Year	Age	Sex	Presenting symptom	Synchronous or metachronous	First sign of RCC?	RCC	Other simultaneous mets?	Fine Needle aspiration	Treatment	Immunohistochemistry
Patey et. al.	1965	63	F	Pulsatile mass x1 year	Metachronous	Y	RCC dx years later	Not discussed	Not mentioned	Radiotherapy and excision	None mentioned
Kucan et. al.	1981	55	M	Mass x3-4mo. on R.	Synchronous	Y	RCC dx on subsequent work up	Not discussed	Not mentioned	Superficial parotidectomy	None mentioned
Sist et. al.	1982	62	M	Mass x2 years on L.	Synchronous	Y	R. RCC dx in subsequent work up	Not discussed	Not mentioned	Deep parotidectomy w/ preservation of the facial nerve	None mentioned
Percival et. al.	1982	71	F	Mass x 3 years on R.	Synchronous	Y	L. RCC dx one year later	Liver, lung	Not mentioned	Surgical excision	None mentioned
Smits et. al.	1984	60	F	Painful mass on R.	Metachronous	N	R. nephrectomy for RCC 8.5 years earlier	Submandibular gland	Not mentioned	Excision of mass	None mentioned
Hessan et. al.	1986	52	M	Mass x2mo. on L.	Synchronous	Y	L. RCC dx in subsequent work up	None at time of parotid presentation, later lungs, ribs, lumbar spine, and brain mets.	Not mentioned	Superficial parotidectomy	None mentioned
Harrison et. al.	1987	64	F	Mass x2mo.on R., R. superficial parotidectomy 4 years prior for "clear cell tumor"	Metachronous	N	Nephrectomy for RCC 10 years prior	None	Not mentioned	Excision of lesions	None mentioned
Owens et. al.	1989	55	M	Mass x3mo. on R.	Synchronous	Y	L. RCC dx in subsequent work up	Chest, brain, bone	Not mentioned	Superficial parotidectomy w/ partial excision of masseter	None mentioned
		75	F	Pulsatile mass x10 weeks on L.	Metachronous	N	R. nephrectomy for RCC 7 years prior	None at time of parotid presentation, later recurrent renal disease.	Not mentioned	Total parotidectomy w/ preservation of the facial nerve	None mentioned
Melnick et. al.	1989	72	M	Mass x2.5 years on L.	Synchronous	Y	R. RCC dx in subsequent work up	Liver, lungs, mediastinum, adrenal	FNA non-diagnostic	Palliative radiotherapy	Positive for vimentin and keratin. Negative for CEA.
Gunbay et. al.	1989	60	M	Painful mass on L. and numbness of L. commisure of lip x1mo.	Metachronous	N	L. nephrectomy for RCC 2 years prior	Not discussed	Not mentioned	Total parotidectomy of mass extending into pterygomaxillary fossa w/ erosion of condylar process of the mandible and the TMJ	None mentioned
Coppa et. al.	1990	42	M	Mass on L. x3 years, pulsatile x1 year, tinnitus x1 mo.	Synchronous	Y	R. RCC dx in subsequent work up	Perirenal lymph nodes	Not mentioned	Superficial parotidectomy w/facial nerve preservation	None mentioned
		55	M	Painful mass x6 weeks on R., bruit	Metachronous	N	L. nephrectomy for RCC 7 years prior	Lungs, axillary lymph nodes	Not mentioned	R. external carotid ligation and multiple partial parotid resections for recurrent bleeding.	None mentioned
Pisani et. al.	1990	59	M	Mass x2mo. on L.	Synchronous	Y	L. RCC dx in subsequent work up	Cerebellar, vertebral	Not mentioned	Superficial parotidectomy w/ preservation of the facial nerve followed by subsequent hemorrhage and several excisions for recurrent disease	None mentioned
Sarangi et. al.	1991	71	M	Mass in L. parotid x3mo at presentation, R. parotid mass presented 4 mo. later.	Synchronous	Y	R. RCC dx in subsequent work up	None at time of parotid presentations, later mets to distal radius.	Not mentioned	L. superficial parotidectomy followed by R. superficial parotidectomy.	None mentioned

Author	Year	Age	Sex	Presenting symptom	Synchronous or metachronous	First sign of RCC?	RCC	Other simultaneous mets?	Fine Needle aspiration	Treatment	Immunohistochemistry
Ravi et. al.	1992	55	F	Bilateral masses x3mo.	Metachronous	N	R. nephrectomy for RCC 7 years prior	Not discussed	Not mentioned	Superficial parotidectomies w/ preservation of the facial nerves on two separate occasions	None mentioned
Borghi et. al.	1995	63	M	Mass x1 year on R.	Synchronous	Y	L. RCC dx in subsequent work up	Liver, pancreas	FNA non-diagnostic	Partial parotidectomy	Positive for vimentin, CAM5.2, AE1. Negative for S-100, CEA.
Sykes et. al.	1995	59	M	Mass x3 weeks on L.	Synchronous	Y	L. RCC dx in subsequent work up	Perirenal lymph nodes	FNA non-diagnostic	Superficial parotidectomy w/ preservation of the facial nerve	None mentioned
Gangopadhyay et. al.	1998	48	M	Mass x3mo. on L.	Synchronous	Y	L. RCC dx in subsequent work up	R. adrenal	FNA non-diagnostic	Superficial parotidectomy	None mentioned
Vara et. al.	1998	50	M	Painful mass x2mo. on L.	Metachronous	N	R. nephrectomy 5 years prior	Not discussed	Not mentioned	Total parotidectomy w/ preservation of facial nerve, locally recurrent in 7mo., repeat excision w/radiotherapy	None mentioned
Adil et. al.	1999	52	M	Mass on R.	Synchronous	N	L. nephrectomy for RCC 5 mo. prior	Post-auricular lymph nodes at time of parotid presentation, later para-aortic, inguinal, and cervical lymph nodes.	Not mentioned	Mass excision, neck dissection	None mentioned
Kundu et. al.	2001	61	M	R. facial weakness and post-auricular pain, R. mass on physical exam.	Synchronous	Y	L. RCC dx in subsequent work up	R. adrenal, bone, skin, pulmonary, cerebral	FNA non-diagnostic	Radiotherapy, pain relief, hospice	None mentioned
Park et. al.	2002	83	F	Mass x2mo. on L.	Metachronous	N	L. nephrectomy for RCC 10 years prior	None	FNA diagnostic	Superficial parotidectomy with preservation of the facial nerve	Positive for vimentin and keratin. Negative for CEA.
Seijas et. al.	2005	67	M	Mass x4mo. on L.	Synchronous	Y	R. RCC dx in subsequent work up	L. adrenal at time of parotid presentation, later lungs, R. adrenal, retroparitoneal lymph nodes	FNA non-diagnostic	Superficial parotidectomy with preservation of the facial nerve	Positive for CAM5.2, AE3, vimentin. Negative for S-100, CK7, CK20, EMA.
Mrena et. al.	2008	58	F	Tender mass on R.	Synchronous	Y	R. RCC dx in subsequent work up	None at time of presentation, R. shoulder mets later identified.	FNA non-diagnostic	Superficial parotidectomy	Positive for CD10, PNRA, vimentin. Partially positive for pan-cytokeratin (AE1/AE3). Negative for calponin, S-100, and cytokeratin-7.
		76	F	R. mass on physical exam	Metachronous	N	L. nephrectomy for RCC 9 years prior	Contralateral kidney, lung, bone	FNA non-diagnostic	Not described	Positive for CD10, PNRA, vimentin. Negative for cytokeratin-7.

Author	Year	Age	Sex	Presenting symptom	Synchronous or metachronous	First sign of RCC?	RCC	Other simultaneous mets?	Fine Needle aspiration	Treatment	Immunohistochemistry
		62	M	L. mass for a few years	Metachronous	N	R. nephrectomy for RCC 5 years prior	None	FNA non-diagnostic	Superficial parotidectomy and selective neck dissection (II-III)	Positive for CD10, vimentin, CAM5.2. Partially positive for CK-8 and CK-18. Negative for cytokeratin-7.
Spreafico et. al.	2008	67	M	R.mass on physical exam	Metachronous	N	R. nephrectomy for RCC 18 mo. prior	Ipsilateral cervical lymph nodes	FNA diagnostic	Total parotidectomy and selective neck dissection (I-V) w/removal of large portion of masseter and inferior facial nerve	None mentioned
Wayne et. al.	2010	61	F	L. mass on physical exam	Metachronous	Y	No primary	Pancreas, skin	Not mentioned	Superficial parotidectomy	Positive for PNRA, vimentin, CD10.
Deeb et. al.	2010	82	M	R. mass x1.5 years, pain	Metachronous	N	Partial nephrectomy for RCC 19 years prior, completion nephrectomy 4 years prior	Not discussed	FNA non-diagnostic	Total parotidectomy	None mentioned

the first sign of renal disease. Review of the cases presented in the literature suggests the most likely presentation is of an asymptomatic, unilateral parotid mass. Associated pain, palpable pulse, bruit, tinnitus, and numbness have been reported but are less common. Somewhat surprisingly, facial nerve weakness is extremely uncommon with only one documented case in the literature [14]. Although most cases of RCC are sporadic, hereditary forms (such as seen with associated with Von Hippel-Lindau disease) have been described and may require screening in high-risk populations.

Fine needle aspiration did not yield a diagnosis all but 3 of the cases reviewed. In this scenario, FNA is commonly non-diagnostic and carries a risk of false positive results. Even if a clear cell tumor is identified on FNA, differentiating the cells from a primary parotid tumor often requires immunohistochemical staining by an experienced pathologist. Differential diagnosis of clear cell tumors of the parotid gland includes clear cell variants of pleomorphic adenoma, myoepithelial carcinoma, epithelial-myoepithelial carcinoma, acinic cell carcinoma, adenocarcinoma of the salivary glands, hyalinizing clear cell carcinoma, mucoepidermoid carcinoma, oncocytoma, odontogenic carcinoma, and metastatic disease [13,38]. Clear cells can also result as artifact in slide preparation.

Immunohistochemistry can be used to distinguish RCC from other clear cell carcinomas of the parotid gland. RCC is known to stain positively for CD10 and vimentin, which were the utilized in the diagnosis of our patient [12]. CD10, also known as common acute lymphoblastic leukemia antigen (CALLA) or neprilysin, is a zinc-dependent metalloproteinase enzyme. Vimentin is an intermediate filament. Both are membranous stains that illuminate the cytoplasmic membrane when positive. CEA is more classically positive in clear cell tumors of parotid origin [12].

Appropriate management options for patients with parotid metastases from renal cell carcinoma is best determined by a multidisciplinary team that includes Otolaryngology, Medical Oncology, and Urology. Therapy for primary renal cell carcinoma ranges from radical or partial nephrectomy [4] to cytoreductive therapy (cryoablation and radiofrequency ablation) and is dependent upon the stage, grade and size of the presenting tumor. Isolated parotid metastasis is also ideally managed by local excision with disease-free margins with facial nerve preservation (when possible). Of the 27 cases in the literature that were managed with local excision, 3 experienced local recurrences [16,24,29]. Recurrence occurred following superficial parotidectomies in all 3 cases, with a disease-free interval of 18 months to 4 years. Two of those patients had untreated renal primaries at the time of disease recurrence [24,29].

Prognosis for patients with parotid metastasis from RCC is difficult to predict due to the limited number of cases reported in the literature. The most important prognostic factor for RCC is pathologic stage. Distant metastasis carries a 1-year survival of 50%, 5-year survival of 5 to 30%, and 10-year survival of 0 to 5%. The presentation of an isolated parotid metastasis is favorable to multiple site distant metastatic spread of disease. Metachronous disease presentation suggests a less aggressive presentation [4]. Review of the literature demonstrated that greater than 50% of the patients found to have parotid RCC had other sites of metastasis. This highlights the need for a thorough metastatic work-up and a collaborative team approach for systemic renal cell carcinoma. Metastatic evaluation includes a chest radiograph, abdominal and pelvic CT or MRI, and liver function tests. Bone scan and chest CT can be reserved for patients with elevated alkaline phosphatase and abnormal chest radiographs, respectively [4].

Conclusions

Renal cell carcinoma (RCC) is a neoplasm with a unique metastatic potential to spread to nearly every organ system in the body. While RCC should not be high on the differential for all parotid gland masses, it should be considered when patients have a history of RCC and when FNA identifies a clear cell tumor. A thorough work-up should be performed, as solitary parotid metastases are rare in the literature and other occult sites may coexist. Isolated parotid disease is best managed with complete surgical excision and facial nerve preservation is usually possible.

Competing interests

The Authors declare that they have no competing interests.

Author contributions

CL was involved in the paper's conception, acquisition of data, drafting and revising of the manuscript. RW was involved in the paper's conception, revising and final approval of the manuscript. Both authors read and approved of the final version of the paper.

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